



The Open-Access Journal for the Basic Principles of Diffusion Theory, Experiment and Application

Intracellular trafficking of lipoplexes: A particle image correlation spectroscopy (PICS) study

Stefano Coppola^{1,2*}, Daniela Pozzi², Giulio Caracciolo², Thomas Schmidt³

¹Department of Anatomy, Histology, Forensic Medicine and Orthopedics,
“Sapienza” University of Rome, Rome, Italy

²Department of Molecular Medicine, “Sapienza” University of Rome, Rome, Italy

³Physics of Life Processes, Leiden Institute of Physics, Leiden University, Leiden, The Netherlands

*stefano.coppola@uniroma1.it

Particle image correlation spectroscopy (PICS) is a powerful and robust analysis technique to investigate the dynamics of molecules with nanometer and millisecond spatio-temporal resolution [1]. This tool allows one to identify and categorize populations within an ensemble of particles, without any a priori knowledge about the dynamics. PICS is here applied to investigate the intracellular trafficking of lipoplexes in CHO living cells. We measured diffusion coefficients and velocities for DOTAP–DOPC/DNA (DOTAP: 1,2-dioleoyl-3-trimethylammonium-propane; DOPC: dioleoylphosphocholine) and DC-Chol–DOPE/DNA (DC-Chol: 3 β -[N-(N,N-dimethylaminoethane)-carbamoyl] cholesterol; DOPE: dioleoylphosphatidylethanolamine) lipoplexes. The results corroborate findings from previous experiments using single particle tracking and spatio-temporal image correlation spectroscopy [2, 3]. PICS allowed us to construct the displacement distributions that displayed clear non-homogeneous behavior. Detailed analyses showed for the first time a strong evidence of lipoplex transitions between active transport (mostly along microtubules) and free Brownian motion in the cytosol. For this latter finding a full theoretical description of intermittent diffusion was developed.

References

- [1] S. Semrau, T. Schmidt: *Particle image correlation spectroscopy (PICS): Retrieving nanometer-scale correlations from high-density single-molecule position data*. Biophysical Journal **92**, 613–621 (2007)
- [2] S. Coppola, L.C. Estrada, M.A. Digman, D. Pozzi, F. Cardarelli, E. Gratton, G. Caracciolo: *Intracellular trafficking of cationic liposome-DNA complexes in living cells*. Soft Matter **8**, 7919–7927 (2012)
- [3] S. Coppola, D. Pozzi, S. Candeloro De Sanctis, M.A. Digman, E. Gratton, G. Caracciolo: *Quantitative measurement of intracellular transport of nanocarriers by spatio-temporal image correlation spectroscopy*. Methods and Applications in Fluorescence **1**, 015005 (2013)